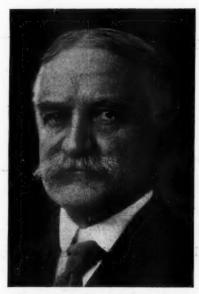
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EDITORIAL

ANTIVIVISECTIONISTS

NTIVIVISECTION has been a "cause" which medical scientists have been forced to combat for years. Like many other things complicating and harmful to human progress and welfare it is based entirely on an appeal to one's emotions rather than to reason. As a consequence the emotionally unbalanced and the misinformed have flocked to its standard. The establishment of a National Society for Medical Research is based on the premise that, if the public understands the truth about the use of animals in medical research and control, little or no support will be given to the antivivisection movement. The work already done in disseminating authentic information to the public explaining the absolute dependence of medical progress on animal experiments is excellent and no thoughtful reader can ignore the facts of the case. These are sufficiently well-known in scientific circles that they require no elaboration. One aspect of the problem has not been fully explored, although it has been commented on by some writers. This is the question as to the factors that cause people to become such ardent supporters of the movement. Here is deep water indeed and even well-balanced persons not antivivisection minded at all are likely to be offended by the facts. Outright and confirmed antivivisectionists will be furious!

Most of the difficulty arises from the fact that cats and dogs are widely used in the experimental laboratories. The use of these animals is essential as everyone knows since lower animals do not generally respond to drugs and techniques as do the higher animals including man. If lizards, snakes or other animals could be and were employed there would be no resentment at all even though these animals were subjected to the most devilish torture conceivable. The trouble then centers around cats and dogs since it is evident that it is not suffering *per se* that principally motivates the antivivisectionists but *dogs* and *cats* that may suffer.

Human beings are sometimes described as nature's greatest error and when one surveys the terrible toll exacted from man by his own self-created environment it is not too difficult to see in this rather June, 1947

cynical description at least a half-truth. A considerable proportion of our people suffer from emotional conflicts. In many it is so evident that they are adjudged insane and restricted in their activities. Many times more than this number, who are institutionalized, are those whose emotional difficulties are so well concealed that they are generally considered sane. The transition from complete insanity to what is described as normalcy is very gradual and classification of a given individual is most difficult indeed.

The love of cats and dogs is a human trait and they have long been a part of man's environment. It may even be said that the experience of caring for such an animal is a beneficial one in developing kindness and consideration in children. The unreasonable love of these animals is, however, a frequent manifestation of some inner conflict which it serves to soothe or modify. Two such instances can be readily described. There is hardly a town of any size that does not possess an elderly maiden lady whose reputation for mothering either cats or dogs is well-known. Frequently the care given her animals is paid for only by penury and self-denial and her meagre savings are left upon her death to perpetuate their care. What is this but the thwarted maternal instinct finding expression? Then, too, many of us have seen the dirty, drunken recluse-completely asocial, living alone with his dogs. Usually they sleep together and eat together. Is this not his human desire for companionship finding some perverted expression?

But someone will say what about the devotion of these animals to their master; devotion that abuse and ill treatment influences not a whit. This is true, but is it not likely that this is the pack instinct finding expression, the pack leader being replaced by man? If so it would be difficult to give dogs credit for the outward manifestation of instinct. They could in fact behave in no other way.

Although the cases cited above are extreme, they illustrate at least two of the cases where an unreasonable degree of affection is placed in animals. In both cases the animals mean more to their owners than do the human beings living as their neighbors. This surely is not a commendable situation nor one that should be permitted to influence unduly society at large. Lesser degrees of the same malady afflict a sizable portion of our population. Middle aged or elderly persons, whose children have left home, often transfer their affection to house pets and so strongly do they love their dog or cat that they are fallow soil for the planting of seeds of antivivisection.

With counter arguments rarely heard it is no wonder that their minds dwell on the alleged suffering of animals and the danger to their own pet which is so loudly heralded. These people, however, when the truth is explained to them are entirely reasonable for they surely love their fellowman and desire to minimize human suffering as much as possible. It is to such people that the data and facts concerning the necessity of using animals should go and the National Society for Medical Research is reaching these and other persons very effectively.

Last but not least some word should be spoken about those promotion minded individuals who like nothing better than to seize upon some program based on emotional appeal and then exploit it for their own advantage. We have and have had many instances of this on our American scene. Such activities are entirely legal and they must, we suppose, continue to be so if democracy is to survive. The only effective measures that can be taken involve the dissemination of truth about the whole matter which is now being done. With this accomplished, scientists can be sure that the citizens of our states and nation will not permit legislation which would bar medical progress and exchange human lives for those of animals. It can be summed up in a few words—which love we the most: animals or our fellowman.



ADJUSTING SOCIETY TO THE SPEED OF SCIENCE *

By Waldemar Kaempffert, D. Sc.**

COMMENCEMENT orators have always impressed upon college graduates the solemnity of the passage from the lecture room to the larger life of the outer world. This is as it should be. I doubt if there has been a more solemn graduation from the Philadelphia College of Pharmacy and Science than this. You pass from academic life not only buoyed with your own high hopes and will to succeed but burdened by our reliance upon you. I can assure you that your graduation means as much to us, your elders, as it does to you. For you are graduating not simply into the world in which we grew up but into a new social era. It is your task not only to carve out careers for yourselves but to mold this new era. Some of us elders are still young enough to be affected by the work that you will do. And it is for this reason that your departure is of vital concern to us.

It is my purpose to contrast the period in which I matured with that which you will shape, to indulge in a few harmless predictions, and to suggest a closer union of the natural and the social sciences, to the end that mankind may guard itself against a recurrence of disaster of the type that has overtaken us time and time again. At the outset I wish to assure you that I realize how hazardous it is to predict what is likely to happen on the basis of what is happening now.

To emphasize this hazard let me read to you part of a letter which was written over a century ago by a French physician, Dr. Alex Guemot. The year was 1832. Europe was in a state of political doubt and economic confusion—both the result of the Napoleonic wars. In fact the situation was similar to our own. A son had been born to Dr. Guemot. What would be the fate of that son in such a world? So Dr. Guemot wrote to a friend:

"I do not know whether to be happy or sorry over the birth of a son . . . The poor infant enters the world in very troubled times. Hardly seventeen years have passed since peace was re-

^{*} Commencement Address, Philadelphia College of Pharmacy and Science, June 11, 1947.

^{**} Science Editor, The New York Times.

stored to Europe, and we still suffer cruelly from the effects of the war. Who knows if my son will not one day be forced to become the citizen of a republic? It makes one shudder. conditions of life are daily becoming more difficult. Nanette, our servant, has paid twenty-three sous for half a kilo of butter and two sous for each fresh egg. It is absurd and exorbitant. I would like to see my son embracing the noble career of medicine, but I see quite well that he cannot. One of the heads of the faculty has confided to me that this profession is literally invaded, and then this madness of speed is wearing out men. Only vesterday I saw a post chaise tearing along. It makes one giddy. The horses were galloping at more than five leagues an hour, and everyone wants his carriage . . . Madness of the century, my dear friend, for which men will pay in the brevity of their days! My son, like his contemporaries, will not live to be old. We know not what the future has in store for him but we can wager with certainty on his not becoming a centenarian."

Nearly every one of these forebodings proved to be false. Contrary to his father's expectation the son became the famous physician Dr. Alex Guemot. He also became the citizen of a republic, and he rode in railway trains and automobiles, at a speed so mad that it would have appalled his parent. To cap the climax this child, which could not possibly become a centenarian, was honored by the French Academy of Medicine on his one hundredth birthday in 1932.

Today we have even more reason to be gloomy than had Dr. Guemot, Senior, in 1832. Already we are talking of a third world war, and we shudder to think what will happen when atomic bombs wipe out whole cities. If I may judge by what the experts in the social sciences tell us the period through which we are passing is not just another period of economic uncertainty. We are faced with problems in international politics and problems in government, and these problems have arisen largely because of the advance of science and technology. Not yet have we fully learned the art of adaptation.

It is the business of the scientist to formulate theories and discover laws that explain nature, and it is the business of the technologist to apply these theories and laws in controlling nature and in fashioning a new environment. Look about you and at yourselves and you will see what I mean. Clothes are unnatural, electric lights are unnatural, street cars are unnatural, automobiles are unnatural. We

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are in the clutch of the machine. Stop the machine and Philadelphia would starve to death in two weeks and disease would be rampant. The whole city is a machine.

The great chemical discoveries and the great inventions of the past all demanded adaptation on our part. Change within science always means social change, and the greater the discovery or invention the greater is that social change. We had to adapt ourselves to science and the machine. Most of our troubles, both national and international, spring from our unwillingness or our inability to adapt our-

selves perfectly.

What do we mean by adaptation? A change in personal habits, a change in folkways brought about by some external agency or influence. The invention of the fountain pen did not change our writing habits and therefore called for no adaptation on our part. But the railway, the steamship, the automobile, the airplane all changed our traveling habits-changed them profoundly. We must adapt ourselves to these new vehicles, at least to those that are operated in the public interest, to the extent that we must obey a timetable. Mass production is impossible without standardization but standardization means adaptation on our part, a willingness to sacrifice individuality. Because of standardization it is becoming more and more difficult to be "different". We dress alike, we eat the same breakfast foods, we buy identical electric lamps, we live in houses that are much alike in their furnishings. The more we discover and invent the more pronounced is this trend toward standardization. In a few decades any marked departure from what the standardized crowd wants and does will be marked as an eccentricity that calls for the intervention of the police and possibly for psychiatric attention. If you think that I exaggerate let me mention the fact that when, about thirty years ago. Raymond Duncan, brother of Isadora, walked down Fifth Avenue in New York, clad in Greek costume and holding his little son by the hand, he was followed by a crowd of derisive hoodlums. Raymond Duncan and his boy were decently clad, and they were behaving themselves. But the police arrested both for disorderly conduct. The hoodlums who were actually disorderly were merely driven off. Ravmond Duncan had departed too far from our standardized fashion in clothes.

New inventions have come out of the war. They will demand more and more adaptation on our part. Very few American families engage in elaborate cooking. They consume tinned or frozen goods, and the foods are the same from New York to San Francisco. In other words, our cooking habits have changed. With the introduction of washable synthetic fabrics I am sure that housekeeping will change. Instead of using even so convenient a labor-saving machine as a vacuum cleaner the housewife of the immediate future will simply turn the hose on a room, dry everything with a blast of hot air—a matter of five minutes. Clothes will probably be woven of water-proofed paper fiber. Price of a suit: \$2.50, tax included. After wearing a suit a week we shall throw it into the waste-paper basket and buy another. We already have paper drinking cups and dishes, but we have not yet descended so low as to use them for anything but picnic meals. In the future we shall use plastic dishes at formal dinner parties—dishes so cheap that we will either throw them away or melt them in superheated water and let them run down the drain.

This civilization is based on the utilization of energy. And yet we have still much to learn about the generation of energy. Perhaps in less than a century our great-great grandchildren will wander through some technical museum and study with amazement a power plant of our time. "And that's how they generated electricity," our descendants will say. "To think that they burned coal wastefully to boil water, then made the steam turn the blades of a turbine and finally made the turbine spin a dynamo! How crude! When all they had to do was to develop thermoelectricity and get energy directly from the furnace."

There will be tremendous advances in synthetic chemistry. You, who have received an admirable training in that subject, must realize what is in the offing. Some day a way will be found to synthesize protein, which means that we shall have the synthetic equivalent of a beefsteak or of white of egg. Synthetic meals will be specially prescribed by doctors for stomachs that cannot digest ordinary food. If we ever succeed in synthesizing albumen we shall be in a fair way of synthesizing life. That will be the supreme achievement of science. But we cannot expect to create anything so intricate as the lowliest oyster. Evolution comes into play. We can expect no more than the creation of a simple cell in the laboratory. We must let that cell evolve for some millions of years before we attain anything higher, and this means the maintenance of some Temple of Biology in which vestal virgins will nurture the man-made cell, like a living flame, gen-

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eration after generation, century after century. No way has yet been discovered of speeding up evolution.

What the social effect of so startling a development may be I do not know. It may be that we shall be able to take our evolutionary destiny in our own hands and decide what we shall make of the human race. But who is to make the decision? The answer must depend on what we expect of social man, and on that question we have not yet made up our minds. That is we have not yet realized fully the need of social adaptation to scientific discovery and invention.

Our confusion is driven home to us by the problem of atomic energy. Is a world state the solution, as many physicists think? If so, we shall be called upon to make the greatest adaptation in human history. Is it the international control of uranium supplies and of the utilization of uranium and plutonium through an International Authority of the kind that Mr. Bernard Baruch has proposed to the United Nations? If so, a yielding of some sovereign rights is demanded, which is again a demand for social adaptation.

Dr. Guemot's gloomy forecast has taught me to be careful. In fact it forces me to extract what comfort I can from the experiments we have thus far made in social adaptation. The electric lights of China, South Africa, Great Britain, the United States are all alike, the automobiles of all countries are more or less alike, the clothes of men and women are more or less alike because Hollywod sets the fashion. These are good signs. If people as far apart as the Chinese and the French, South Sea Islanders and Americans, Englishmen and Central American Indians handle and use the same things, they naturally think of these things in the same terms.

Ultimately this thinking alike can carry the world far. It will dawn on the different nations, I think, that it is sheer folly to restrict international airplanes to certain routes so that fortifications may not be photographed and that we cannot make the most of science if important discoveries are kept secret for military reasons. The first and easiest step in improving international relations is to develop some system of international research under the auspices of the United Nations and to disseminate the results to the uttermost parts of the earth by radio, by the motion picture, by the printed word. It will be discovered, then, that, as I have said before, change within science always means social change. When we learn that lesson we shall study the social changes and even predict some of the more important,

which in turn means that we shall have time to prepare ourselves for such economic upheavals as those that followed the introduction of synthetic dyes and of synthetic ammonia. In a word, we must learn the art of social adaptation. It is because we have not learnt it that we are still grappling with the problem of atomic energy, still preparing for war.

You have been trained in science. That is you have acquired the scientific habit of mind. Anyone who has acquired that habit must realize the need of social adaptation. You are pioneers of a new social era. It is not we but you who will fashion the world anew. There is work for you to do—real constructive, engineering work, with humanity as your raw material, human aspirations as your forces, and social happiness as your final product. Rise and do that work! It is your supreme duty not merely to gain a foothold for your individual selves but to create a better world than we knew, to mold human destiny. For us the night begins to fall. We are the sunset. You are the sunrise of a new social day.

THE IMPORTANCE OF CREATINE AS GROWTH FACTOR IN RATS *

By Saul Caspe

In the cell growth of chick, mouse, rat and human tissue in tissue culture. While these results indicate that creatine is an amino acid necessary for developmental growth as some indirect evidence suggested, they do not harmonize completely with the conclusion of some prior experimental work in vivo. Chanutin (2) and Chanutin and Beard (3) who studied growth of rats and mice for two months, feeding them various amounts of creatine, concluded that creatine has no effect upon the growth curve. These experiments reported in 1927 and 1928 were complicated by the use of an adequate diet supplemented with creatine, by the utilization of a yeast for the source of B vitamins, and by the selection of rats whose initial weights were over 70 grams. These authors also observed that creatine in the muscle reached a maximum regardless of the amounts of creatine in the diet and the duration of the experiment. Obviously the creatine added to their adequate diets was in excess of the body needs.

Recently Sure and Ford (4) have demonstrated that in thiamine and riboflavin deficiency, there occur large excretions of creatine in the urine. For our purposes, it was deemed advisable to reduce the creatine body level first, in order to observe the effect upon growth of creatine fed subsequently. A subminimal level of body creatine could be achieved by depleting rats of their store of B₁ or riboflavin or both. By feeding a vitamin deficient diet containing an inadequate amount of protein or amino acids we will find a growth base line from which effects of added vitamins and creatine can be observed.

The experiment was divided into two parts. In the first part white male rats weighing 40-48 grams were fed the diet (slightly modified) reported by Kinsey and Grant (5) but instead of ten essential amino acids nine were used (arginine monohydrochloride being excluded) at a 5.4% level, and a vitamin free casein was added at a 5.4% level to these amino acids. All the other materials of this diet were also added except thiamine hydrochloride. The rats were kept

^{*} Caspe Laboratories, 490 West End Avenue, New York 24, N. Y.

on this B_1 depletion diet for seven days during which time they failed to grow or even lost weight. Preliminary experiments indicated that rats which continued to gain more than two grams in weight after seven days of a depletion diet are unsuited for the test and should be kept on the depletion diet for a longer period or discarded. After the seven day depletion period, the rats were divided into four groups and fed supplements as follows:

- I. controls
- 2. daily dose of 50 mg. creatine
- 3. daily dose of 10 μ g. and 20 μ g. thiamine hydrochloride
- 4. daily dose of 10 μ g. and 20 μ g. thiamine hydrochloride plus 50 mg. creatine.

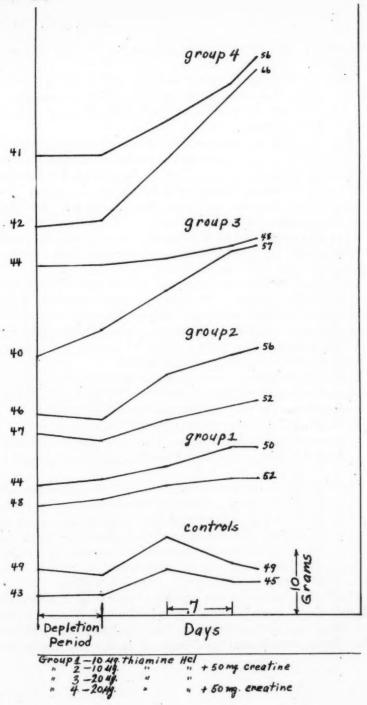
The rats were given these supplements for seventeen days. After the seventeen days, the controls gained 3.3%, the creatine fed rats gained 6.3%, the 10 μ g. of thiamine fed rats 8.6%, the 10 μ g. of thiamine plus 50 mg. creatine fed rats 18.7%, the 20 μ g. of thiamine fed rats 19.3% and the 20 μ g. of thiamine plus 50 mg. creatine gained 42.5% in weight. The growth curves of the individual rats are shown in the graph.

In the second part of the experiment white male rats weighing approximately 35-40 grams were fed the following B₁ and riboflavin deficient diets.

DIET I		DIET 2	
Creatine	2.5 grams	Glycine	1.4 grams
Casein	7.0 grams	Casein	7.0 grams
Salt mixture	4.0 grams	Salt mixture	4.0 grams
Cod liver oil	2.0 grams	Cod liver oil	2.0 grams
Corn oil	10.0 grams	Corn oil	10.0 grams

Starch was added to both diets to make 100 grams of feed. The amount of glycine is approximately equivalent to the glycine content of the creatine used.

The control rats were also fed Diet 1. On the eighth day two glycine rats showed signs of bilateral denuded areas and five rats showed foreleg sores. On the ninth day two more glycine rats showed bilateral denuded areas. All glycine rats had mild nasal



hemorrhages. In contrast, two of the creatine rats had only mild foreleg sores.

From the tenth day on all rats were fed daily 50 μ g. of nicotinamide and 20 μ g. of pyridoxine hydrochloride. With the exception of the control rats, all other rats were given daily 20 μ g. of thiamine hydrochloride in addition.

Beginning with the eighteenth day all rats excepting the controls were given daily 10 μ g. supplements of riboflavin although the creatine rats had shown no lesions. The glycine rats were manifesting greater areas of denudation and were failing to gain weight. The bodies of two of these rats were more than $\frac{3}{4}$ denuded. The riboflavin addition was continued for ten days. The creatine rats continued to gain weight and grow physically as well as sexually, while the glycine rats did not. However, the denuded areas improved somewhat with the riboflavin supplement.

In Table 1 are given the weights of the individual rats and their per cent increase in weight. The control rats lost considerable weight but showed no evidence of lesions. One of the glycine rats showed evidence of cataract formation and improper gait—dragging hind legs. Apparently lack of creatine plays a role in the onset of symptoms and may play a part in the therapy of these lesions.

After the conclusion of the experiment tabulated in Table I, the experiment was continued for another ten days by feeding the rats the same supplements but interchanging the diets: those rats fed Diet I were changed to Diet 2 and those fed Diet 2 were changed to Diet I.

The rats changed to Diet 2 showed a loss of weight of 6.2% while those changed to Diet 1 (creatine) showed a gain of weight equal to 23%.

Another experiment was conducted in which all experimental animals were fed Diet 2 (glycine diet) during the 12 day depletion period and then those rats with symptoms of severe alopecia were given the Diet 1 (creatine diet) while the others were continued on Diet 2. All rats were also given daily supplements of nicotinamide, pyridoxine, riboflavin, thiamine, choline and Ca Pantothenate for 28 days. The gain in weight for the individual rat is recorded in Table 2.

Again, the creatine fed rats depleted of their store of B vitamins and maintained on an inadequate protein diet gained more weight when vitamin supplements were given than the glycine rats maintained under similar experimental conditions. It is also noteworthy that

LABLE 1

Remarks	No lesions opacity of eyes	Il have denuded area and opacity	of eyes		No lesions				
Increase Weight	-2e -17	0 14	++	+	+23				
% Increase After 10 Days % in Weight Riboflavin in Weight	37 29	43	33	41	53	53 *	39	40	50
% Increase in Weight	- 3.0 - 2.7	- 2.6	+ 5.6		+ 9.3	+12.2	+12.1	+14.2	+14.6
After 8 Days Supplement Weight	4 %		9 4 6				37	. 40	47
After 10 Days Depletion Diet Weight	35	44 86	39	40	43	41	33	35	41
Initial Weight	46	43	98 88	40	41	38	33	38	40
Rat Number	22	33	36.35	37	44	45	46	47	48
	Controls Diet 1	Diet 2	(Glycine)		Diet 1		(Creatine)		

Controls were fed supplements of only nicotinamide and pyridoxine daily after 10th day.

Glycine and Creatine rats were given 50 µg. nicotinamide and 20 µg. pyridoxine hydrochloride daily after 10th day.

Glycine and Creatine rats were given 20 µg. thiamine hydrochloride daily for 8 days.

Glycine and Creatine rats were given 20 µg. thiamine hydrochloride plus 10 µg. riboflavin daily for final 10 days.

TABLE 2

					0														
	Remarks	Opacity of eyes.		All had denuded areas	after depletion pe-	riod. Improvement	marked at conclu-	sion of experiment.			Rat 75 - No Symp-	toms.	Rat 71, 74, 76-	Slightly denuded	areas.	Rat 70, 72 & 73-alo-	pecia progressively	worse throughout	experiment.
	% Increase in Weight	—I3	-29	+56	+24	+42	+18	+33	+31	+33	- 3	+3	1	9 +	+3	8 +	9 +		
ifter 28 days of	Supplements Weight	39	32	4	41	47	39	48	46	4	32	33	35	38	36	39	36		
After 12 days After 28 days of	Depletion Diet Supplements Weight Weight	46	45	35	. 33	33	33	36	35	33	33	32	35	36	35	36	34		
	Initial	4	. 46	35	33	35	34	35	36	3 28	34	32	35	36	36	37	34		
	Rat	29	89	99	19	62	63	64	. 65	98	20	71	72	73	74	75	92		
		Control	Diet r	Diet 2	Changed to Diet 1	After Depletion	Period.	Diet I (Creatine)			Diet 2	(Glycine)							

Controls were fed supplements of only 50 µg. nicotinamide, 20 µg. pyridoxine hydrochloride, 2 mg. choline chloride and 1 mg. Ca Pantothenate daily after 12th day.

Glycine and Creatine rats were fed the same plus 20 µg. riboflavin and 20 µg. thiamine hydrochloride after 12th day.

symptoms of alopecia improve considerably on a creatine diet, but not on a glycine diet.

In another series, the growth of rats fed Diet I (creatine) was compared with the growth of rats fed the following diet containing the alpha nitrogen equivalent of creatine in the form of d-glutamic acid and designated Diet 3:

		DIET 3		
d-Glutamic	Acid		2.8	grams
Casein			7.0	46
Salt Mixt	ure		4.0	66
Cod Liver	Oil		2.0	66
Corn Oil			10.0	44

Starch was added to make 100 grams of feed.

Both groups of rats were kept on a depletion diet for 12 days, and then were fed daily vitamin supplements for 29 days. The results indicate that those rats, depleted of their store of B vitamins, grow at a somewhat accelerated rate on the creatine (protein deficient) diet as compared with the rate of growth of rats maintained under similar experimental conditions on a d-glutamic acid diet, (when both groups were fed vitamin supplements). The results appear in Table 3.

It was deemed advisable to compare creatine and arginine as growth promoters. Young rats were placed on a basic protein deficient diet as follows:

DIET	A	(Contro	Diet)
DILL	4	Contro	i Dice,

Casein	8 grams
Salt Mixture	
Cod Liver Oil	2 * "
Corn Oil	10 "
Choline Chloride	0.13 "
Ca Pantothenate	0.015 "

Starch was added to make 100 grams of feed.

After the depletion period, two rats were sacrificed for the purpose of making creatine determinations of tissues, and two other rats were continued on the Control Diet but were fed vitamin supplements by catheter. The rest of the animals were divided into two groups fed the following Diets:

TABLE 3

Remarks	Opacity of eyes. Rat 88 and 89 totally blind before death.		No symptoms observed.		Rat 90, 91, 94, 96 and 97 had slight denuded areas after depletion	period. Alopecia in- creased during ribo- flavin period. Rat 93	snowed advanced symp- toms of alopecia which developed during this period.
% Increase in Weight		41.0	30.5	33.3 42.9	33.3 19.5 34.2	20.0 18.9 28.9	13.9
After 12 Days After 8 Days After 21 days Depletion Diet Supplement Riboflavin Weight Weight	36 died 17th day 30 died 15th day	84 4	52 47	22 4 05	8 6 4 1 1	444	43
After 8 Days t Supplement Weight	35	36	37	39	% 4 % % % 6 % % % % % % % % % % % % % % % %	1823	37
After 12 Days After 8 Day Depletion Diet Supplement Weight Weight	37	36	9,9,	3333	8 14 % 8 8 4 9 8	3873	36
Initial Weight	36	36.55	33.33	35	3,8,8,3	32 33	36
Rat Number	88 86	08 8 18	8 8 8	× × × ×	0 0 1 0 0	8 4 50	66 66
	Control Diet 1		Diet r	(Creatine)		Diet 3 (Glutamic Acid)	

Controls were fed supplements of only nicotinamide and pyridoxine hydrochloride daily after 12th day.

Glutamic Acid and Creatine rats were given 50 µg. nicotinamide and 20 µg. pyridoxine hydrochloride daily after 12th day. All experimental rats were given 20 µg, thiamine hydrochloride daily for 8 days.

All experimental rats were given 20 µg. thiamine hydrochloride, 2 mg. choline chloride, 1 mg. Ca Pantothenate and 15 µg. ribcsavin daily for final 21 days.

DIET 5		
Casein	7.5	grams
Creatine	2.0	66
Salt Mixture	4.0	66
Cod Liver Oil	2.0	66
Corn Oil	10.0	66
Choline chloride	0.13	66
Ca Pantothenate	0.015	4.6
DIET 6		
Casein	7.5	grams
<i>l</i> -Arginine HCl	3.2	44
Salt Mixture	4.0	44
Cod Liver Oil	2.0	44
Corn Oil	10.0	44
Choline Chloride	0.13	66
Ca Pantothenate	0.015	4.6

Starch was added to make 100 grams of feed.

These rats were also fed daily vitamin supplements by catheter. At the conclusion of the experiment the animals were sacrificed and creatine analysis made of heart, leg muscle, and testes according to the technique of Rose, Helmer, and Chanutin (6). The results are represented in Tables 4 and 5.

Discussion

In our work arginine was eliminated from the Kinsey-Grant diet because this pseudo-essential amino acid may yield sufficient creatine to offset any real comparison between rats fed no creatine and others fed creatine. From the results obtained in these studies it appears that young rats, depleted of their store of B vitamins and maintained on an inadequate amino-acid diet, grow at an accelerated rate when fed the vitamin supplements plus creatine as compared with those rats fed the same vitamin supplements alone (refer to growth curves).

The results obtained using glycine seem to parallel those obtained by Kinsey and Grant and we concur with their opinion that "more than the mere addition of a source of nitrogen is required for good growth." Creatine, fed to rats under the experimental regimen herein reported, has a stimulating effect upon growth.

TABLE 4

Average 31 32.5 Average 34 32 Average 31 32.5 ed to 102 30 33 d to 102 30 33 d to 106 30 33 Average 31.7 34.9 2 days depletion 104 32 33 3 days depletion 104 32 33 44.5 52 53 518th 42 Average 31.7 34.9 518th 43 52 days depletion 104 32 53 days depletion 104 32 54 days depletion 104 32 55 days depletion 104 32 6 days depletion 105 32 6 days days days days days days days days					Atter 22 days	% Increase	
98 934 335 Average 31 100 34 46 53 115 100 34 46 53 115 114 47.5 114 49 94 34 34 35 49 40 40 95 30 31 32 49 40 40 95 30 31 40 40 95 40 40 40 40 40 40 40 40 40 40 40 40 40	Diet	Kat No.	Initial wt.	pletion diet wt.	Supplements wt.	in Weight	Kemarks
98 34 33 Average 28 32-5 Average 31 32-5 100 34 46 53 15 101 38 37 42 15 47.5 47.5 14 days depletion 92 29 31 32 49 94 34 41 49 20 95 30 34 34 96 31 34 34 96 40 40 97 32 29 31 49 98 30 34 99 31 34 90 32 20 90 34 41 90 40 20 90	ontrol					,	
Average 28 32 Average 31 32.5 100 34 46 53 15 101 Average 36 41.5 42 113 41.5 42 114 41.5 47.5 114 42.6 113 43.8 35 43 43.8 34 44.3 26 44.3 27 44.4 32 44.3 27 44.5 27 44	iet 4	80	34	.33			
Average 31 32.5 Average 31 46 53 15 IOI Average 36 41.5 42 13 d to 90 34 35 49 40 93 29 32 49 40 94 34 41 49 20 95 30 34 41 49 20 96 31 36 41 41 49 20 Average 31.7 34.9 44.3 27 1 to 102 30 33 53 60 1 days depletion 104 32 31 40 60 IOS 30 34 42 42 Average 33.3 36 52 53 Average 33.3 36.7 45.5 24		.00	28	32			
too 34 46 53 15 Average 36 41.5 47.5 14 d to 90 34 35 44 d days depletion 103 32 34 d to 102 30 33 33 d to 102 30 33 33 d to 102 30 33 33 d days depletion 103 32 33 Average 33.3 36.7 45.5 24 Average 33.3 36.7 45.5 24		Average	31	32.5			
to to go 34 46 53 15 Average 36 41.5 47.5 14 days depletion 92 29 31 32 43 40 99 34 35 49 40 93 29 31 32 34 94 44 41 49 20 95 30 34 443 27 1 to 102 30 33 33 60 1 days depletion 104 32 33 60 1 days depletion 104 32 33 60 1 days depletion 104 32 33 34.9 40 29 1 days depletion 104 32 34 44.3 55 24 Average 33.3 36,7 45.5 24	ontrol))				
d to 90 34 35 47 42 13 Average 36 41.5 47.5 14 days depletion 92 29 31 32 49 93 29 31 32 49 94 34 41 41 49 95 30 34 34 140 102 30 33 33 150 42 44.3 27 160 30 34 42 Average 33 34.9 44.3 27 170 Average 33 35 41 170 Average 33 35 36 171 Average 33 35 36 172 42 42 173 44 42 174 45 175 42 175 42 177	iet 4	100	34	46	53	15	Marked Alopecia
Average 36 41.5 47.5 14 d to 90 34 35 49 40 g days depletion 92 29 31 32 49 94 34 41 49 20 95 30 34 43 27 95 31 36 51 42 Average 31.7 34.9 44.3 27 d to 102 30 33 53 60 e days depletion 104 32 31 60 105 30 34 42 61 107 Average 33.3 36.7 45.5 24		101	38	37	42	13	Slight denuded area
d to 90 34 35 43 26 40 40 92 92 92 31 32 32 33 94 94 94 94 94 94 94 94 94 94 94 94 94		Average		41.5	47.5	14	
d to 90 34 35 43 26 days depletion 92 29 31 32 49 40 93 29 32 49 40 94 34 41 49 20 95 30 34 41 49 20 95 30 34 44 3 27 Average 31.7 34.9 44.3 27 1 to 102 30 33 33 60 1 days depletion 104 32 33 60 1 days depletion 104 32 34 44 45 52 1 to 106 30 34 44 42 55 24 Average 33.3 36.7 45.5 24	ontrol				:		
t days depletion 91 33 35 49 40 40 93 29 31 32 32 34 99 99 99 99 99 99 99 99 99 90 90 90 90	iet 4 Changed to	06	34	35	43	56	
t days depletion 92 29 31 32 3 94 34 41 49 34 34 34 95 30 34 49 30 30 31 35 34 44.3 27 37 34 44.3 27 37 34 34.9 44.3 27 37 37 32 33 32 33 32 33 32 33 32 33 32 33 32 33 32 33 32 33 32 33 32 33 32 33 32 33 34.9 42 42 5 24 44.3 27 44 42 5 24 44.3 32 32 33 35.7 45.5 24 24 25.5 24		16	33	335	49	40	
93 32 43 34 34 99 99 99 99 99 99 99 99 99 99 99 99 99	iet 5 after 12 days depletion		29	31	32	3	Slight denuded area
94 34 41 49 20 95 30 34 43 27 Average 31.7 34.9 44.3 27 1 to 102 30 33 53 60 1 days depletion 104 32 31 60 105 30 34 52 29 106 30 34 52 53 107 42 42 45 109 33 35 41 17 Average 33.3 36.7 45.5 24		93	29	32	43	34	Slight denuded area
95 30 34 43 27 96 31 36 51 42 Average 31.7 34.9 44.3 27 1 to 102 30 33 33 53 60 1 days depletion 104 32 31 40 29 105 30 34 52 51 42 103 32 33 53 60 105 30 34 40 29 107 42 40 45 108 37 44 42 —5 109 Average 33.3 36.7 45.5 24		96	34	41	49	20	Slight denuded area
96 31 36 51 42 Average 31.7 34.9 44.3 27 1 to 102 30 33 33 53 1 days depletion 104 32 31 60 105 35 42 61 45 106 30 34 52 53 107 37 44 42 —5 Average 33.3 36.7 45.5 24	reatine Diet	95	30	34	43	27	
Average 31.7 34.9 44.3 27 1 to 102 30 33 33 53 60 1 days depletion 104 32 31 60 1 105 30 34 52 53 1 107 37 44 42 —5 1 109 33 36.7 45.5 24		96	31	36	51	42	
1 to 102 30 33 33 0 0 0 103 32 33 0 0 103 32 33 53 53 60 103 32 31 40 40 29 105 30 30 34 52 53 53 109 109 37 44 42 425 109 109 33 3 36.7 45.5 24		Average		34.9	44.3	27	
1 to 102 30 33 33 00 0 0 0 0 0 0 0 0 0 0 0 0 0	ontrol						
103 32 33 53 60 104 32 31 40 29 105 35 42 61 45 106 30 34 52 53 107 37 42 42 61 108 37 44 42 62 109 33 35 44 42 62 Average 33.3 36.7 45.5 24	iet 4 changed to	102	30	33	33	0	Pronounced Alopecia
1 days depletion 104 32 31 40 29 29 105 35 42 61 45 106 30 34 52 53 107 37 42 44 42 0 0 109 33 35 44 45.5 24			32	33	53	9	Denuded area
105 35 42 61 45 106 30 34 52 53 107 37 44 42 0 109 33 35 41 17 Average 33.3 36.7 45.5 24	iet 6 after 12 days depletion		32	31	40	29	
106 30 34 52 53 107 37 42 42 0 108 37 44 42 —5 109 33 35 41 17		105	35	42	19	45	Pronounced Alopecia
107 37 42 42 0 108 37 44 42 —5 109 33 35 41 17 Average 33.3 36.7 45.5 24		901	30	34	525	53	Slight denuded area
108 37 44 42 —5 109 33 35 41 17 Average 33.3 36.7 45.5 24	rginine Diet	107	37	42	42	0	Slight denuded area
33 35 41 17 Average 33.3 36.7 45.5 24		108	37	44	42	5	Slight denuded area
33.3 36.7 45.5		100		35	41	71	Denuded area
		Average		36.7	45.5	. 24	

Creatine and Arginine and control rats 100 and 101 were given 50 µg. nicotinamide, 20 µg. pyridoxine hydrochloride, 20 µg. thiamine hydrochloride and 15 µg. riboflavin daily for 22 days.

TABLE 5

TOTAL CREATININE (CREATINE PLUS CREATININE) OF TESTES AND LEG MUSCLE EXPRESSED IN mg. OF CREATINE PER 100 gm. OF TISSUE

Type Rat No. 98 99 99 99 99 99 99 99 99 99 99 99 99		Testes Creatine		Testes Total	Muscle-Creatine
98 99 99 90 92 93 93 94 95 96 102 103 104 106 110	. Animal wt.	mg./100 gram.	Testes wt. gram	Creatine mg.	mg./100 gram.
99 Supplement 101 92 93 94 94 95 96 102 103 104 105 110 111	33	182	0.275	0.501	453
Supplement 101 92 93 94 95 96 102 103 104 105 110 111	32	202	0.257	0.519	368
Supplement 101 92 93 94 95 96 102 103 104 105 106 110	53	310	0.086	0.266	302
92 93 94 95 102 103 104 105 106 110	42	236	0.265	0.625	531
93 94 95 96 102 103 104 105 108 110	32	428	0.086	0.366	519
94 95 96 102 103 104 106 107 110	43	233	0.159	0.370	200
95 96 102 103 104 105 106 110	49	272	0.237	0.646	267
96 102 103 104 105 106 110	43	308	0.130	0.400	472
102 103 104 105 106 107 110	51	293	0.267	0.784	384
103 104 105 106 107 110	33	311	0.063	961.0	397
104 105 106 107 110	53	258	0.281	0.724	453
105 106 107 108 110	40	. 239	0.239	0.570	333
901 701 801 111	19	376	0.200	0.784	287
108 110 1111 1111	52	332	0.108	0.360	344
108	42	257	0.133	0.342	212
111	42	216			292
III	78	246	0.343	0.844	367
	153	961	1.538	3.570	345
Normal 112 150	150	161	1.262	2.408	311

In all other experiments reported (see tables), growth comparisons were made between rats on a protein deficient diet plus creatine and rats on the same basic diet plus the alpha nitrogen equivalent of creatine in the form of glycine, d-glutamic acid or l-arginine hydrochloride.

The results indicate that in these comparisons creatine manifests growth stimulating activity somewhat greater than that of glycine or d-glutamic acid. It is significant that this activity of creatine is more pronounced only when young rats weighing 35-40 grams are used, and when supplemental vitamins are fed in minimum doses.

The biochemical and biological intimacy of creatine and arginine perhaps explains the similarity of growth stimulation when one is substituted for the other as was done by us on the Kinsey-Grant diet. In fact, it has been postulated, based on presumptive and some direct evidence, that arginine is a precursor of some muscle creatine. Therefore the comparison between arginine and creatine as growth stimulators is of particular interest (See Table 4). Both of these amino-acids seem to be equally efficacious in this respect. Creatine, however, is more effective in preventing pronounced alopecia.

There are indications that maintenance of a creatine body level is important not only as a growth factor but also in the prevention of

symptoms produced by B vitamin deficiencies.

Bodansky (7) showed that administration of 50-100 mg. creatine to rats markedly increased the creatine concentration of the liver in rats and after 12-24 hours the liver creatine content declined to essentially normal values. Under the conditions of our experiment the creatine level of testes was higher in each of the creatine and arginine rats as compared with the average for controls #98 and #99. Only one creatine rat #93 showed a testes creatine level less than the average of the two control rats #100 and #101 receiving vitamin supplements. In general the faster growing rats in both the creatine and arginine series showed the highest testes creatine level as well as the total creatine in the tissue.

It is interesting in this connection to compare the testes creatine levels of the experimental rats with those normal litter mates which were kept on a stock diet from the inception of this experiment. Rat #110 was sacrificed at the same time with controls #98 and #99 while rats #111 and #112 were sacrificed at the conclusion of the experiment. Comparing Rats 94, 96, 103 and 105 with 110, indi-

cates that while their average weight is only 53 grams in contrast to 78 grams of the normal rat, the testes creatine level is higher and the total creatine content of the testes approaches that of the normal rat. It seems as the testes grow the creatine level for this organ drops. (Compare the 3 normal rats.) Since testes creatine levels of growing animals have not been determined, it might be advantageous to study the amount of creatine in this organ throughout the growing period.

Summary

When thiamine and creatine supplements were given to rats fed a modified Kinsey and Grant amino-acid diet deficient in B₁, their growth was accelerated as compared with those receiving thiamine supplement alone.

Rats fed an inadequate protein diet deficient in thiamine and riboflavin showed an accelerated growth, when fed these vitamin supplements and creatine, in comparison with rats fed the same vitamin supplements and either glycine or d-glutamic acid.

Creatine or arginine produce the same degree of growth acceleration in rats fed protein or amino acid deficient diet containing minimum doses of the B complex.

The testes creatine level in young growing rats seems to be affected by either creatine or arginine.

Note: The author expresses appreciation to Professor Robert Chambers for his suggestions in presenting this paper, and is thankful to Dr. G. K. Falk for his cooperation in some of these studies.

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PROGRESS OF BRITISH PENICILLIN *

By Rosemary Denston, B. Pharm., Ph. C.

THE news that the sodium salt of penicillin is now available in crystalline form for use in cases where maximum purity and stability are essential, marks another step forward in the antibiotic field. From the time of Sir Alexander Fleming's discovery in 1929 progress has, in the main, been steady. It is now rapidly accelerating; but when the results of several years' work are condensed into a brief article, an impression of ease may result, exceptionally misleading in the case of penicillin. This substance has from the start proved singularly difficult to handle. The crystalline form, for instance, was made, only after many failures, by forming an organic base of the penicillin and then converting this to sodium salt. This process, though it has been known for some two years, has only recently been adapted for mass-production. It was, however, a most important discovery. Crystalline Penicillin Glaxo contains at least 90 per cent. of Penicillin II—that is, G—and the material has exceptional stability.

The advantages of the crystalline penicillin are very marked, especially in brain surgery, for it can be used in extreme concentration without risk of irritation. As permissible dosage increases, the powers of the drug appear sometimes even greater than was at first predicted. There is every reason to think that with the progress of research still more remarkable results in healing will be obtained.

The role played by British Laboratories was and remains part of the penicillin story. By 1941 the paramount value of penicillin, above all in war surgery, was established beyond doubt, but Britain, then under constant threat of invasion, and already straining her resources to the utmost, could not undertake large scale development of the drug. Research on mass production techniques was therefore transferred to the United States. Unfortunately, however, the submerged culture process, involving huge tanks, though plainly superior to "jug and bottle" methods, was obviously a long-term policy, whereas the vital need for the drug was now. In 1943, with D-day already foreshadowed, Glaxo Laboratories, whose research staff had been at work on penicillin problems from an early stage, received instructions from the British Government to obtain the greatest possible immediate output.

^{*}Contributed through British Information Services, 30 Rockefeller Plaza, New York, N. Y. (212)

Surface Culture or Single Unit Method

Since 1941 experiments and production had been based on the surface or single unit method, which consisted of growing the mould in a flask, from which, after seven to nine days, the active liquid could be harvested. So far little more than experimental quantities had been made in this way; but in February 1943, by simply multiplying single-flask technique, Glaxo became the first to start production of penicillin on a truly commercial scale.

During World War II, at least 80 per cent. of British penicillin was produced by these laboratories, one factory alone handling 300,000 separate flasks. Though quality was the need, quality with quantity was the aim, and it was not long before an 80 per cent. pure product was consistently maintained.

In 1945, a British team of chemists, profiting from considerable experience in the use of the freeze-drying technique for other preparations, adapted and finally perfected this process for use in the final stage of penicillin production—the drying of the purified sub-



· Semi-automatic filling of the vials with a concentrated solution of penicillin prior to freeze-drying. Aseptic precautions maintained throughout. (Glaxo Laboratories Ltd.)

stance. Ultimately the whole Glaxo penicillin output was freezedried at the main factory. A minor diversion occurred here, when a flying bomb hit the drying plant section, and buried some of the plant. The devastation was considerable, but production was resumed in 24 hours.

Considerable as the success with surface methods had been, deep culture had such obvious advantages over the single-unit technique that early in 1943 a special Fermentation Division of the Company had been formed. With the cooperation of Britain's Ministry of Supply, a site was secured for a new factory to be devoted entirely to the production of penicillin. Building was begun shortly after the war ended, and despite the many difficulties of that period production was begun seven months later, at the beginning of 1946.

Made Future Quantity-Supplies Assured

British production figures as a whole had been mounting steadily, but the advent of, first, the new Glaxo factory at Barnard Castle, a picturesque old north country mill town, and then the factory of the Distillers' Company at Speke, near Liverpool, made future quantity-supplies assured.

During the rapid progress in the production of penicillin by fermentation, a team of British and American chemists were attempting to discover the exact chemical structure of the drug. This work, it was hoped, would not only help to explain its unique properties, but make possible its synthesis. Research showed that there were at least four penicillins, all with the same basic formula but with slight variations in the side chain. They were named F, G, X and K in America, but in England are known as Penicillins I, II, III and IV.

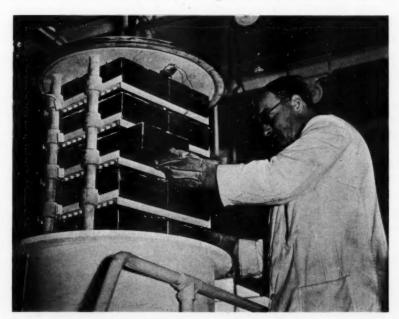
Penicillin I was the form obtained in largest quantity when, as in the first surface culture techniques, entirely synthetic food was provided for the mould. Penicillin II is formed in quantity by both deep and surface culture if the "food" contains corn-steep liquor—a by-product of the starch industry. Penicillin III occurs in small quantities from all corn-steep liquor methods of manufacture, but since it is not readily soluble in chloroform (a usual method of extraction) it is generally eliminated from the final product. Penicillin IV is formed mainly by deep culture production with the newer

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mould strains. It seems curiously ineffective therapeutically, probably owing to its rapid destruction by the body. Fortunately research workers were quick to realize this. Changes were made in the "foods" and in the processes of extraction, so that now Penicillin IV is present in only very small proportions, Penicillin II predominating in the final Glaxo product. Dihydro-Penicillin F is a more recent discovery and probably the fore-runner of other penicillins.

Five Times Standard Legally Required

Even in surface-culture days, British chemists maintained a level of purity between four and five times that of the standard legally required. At the present time this is 300 units per milligram, and penicillin Glaxo has invariably a strength of at least 1,200 to 1,500. When the International Standard was established, and it became desirable that a quantity of standard substance of similar purity should be available in Britain, it was thought at first that there was not



Loading stainless steel trays containing vials of penicillin into the apparatus for freeze-drying the drug. After loading the head of the apparatus comes down into the cylinder below and high vacuum is applied. (Glaxo Laboratories Ltd.)

enough penicillin of the requisite quality. Glaxo Laboratories, however, were able to provide 30 grams of material at the necessary purity level, and the actual penicillin now in use as a British standard has a potency of 1,600 units per milligram.

The maintenance of a high standard of control depends to a great extent on assay technique. This is a field too complex for brief discussion, but one in which the British team have done good work. In particular, a most useful modification of the *Staphylococcus aureus* plate method was devised in the Greenford Laboratories. At

Barnard Castle, research is progressing steadily.

Meanwhile, chemists and biologists are pushing ahead, seeking for other mould-produced substances which may prove effective against conditions not affected by penicillin. Eventually science may succeed in harnessing the defense substances of many small organisms for the defense of man—and this on such a scale that even our most stubborn ills will be finally conquered.



Photograph showing valves controlling the air, steam and water of the 5,000 gallon fermenter tanks in the submerged culture method of production of penicillin. (Glaxo Laboratories Ltd.)

RELINING THE AMERICAN STOMACH

By T. Swann Harding

N OT long ago a prominent physician remarked that he had great difficulty in believing certain diseases to be caused by modern food and eating habits, though they were habitually attributed to these. For the diseases were not more but less prevalent among our ancestors who both ate and drank more immoderately, more irregularly, and more persistently than we. Diet habits have changed enormously in recent times and stomachs now get a modern lining.

The reader of Pepy's Diary is repeatedly astounded at the eating habits of Samuel, his wife, and their entire circle of acquaint-ances. Whenever the ravenous fury came upon them they would procure stupendous quantites of food, cook it and eat it gluttonously, whether at midnight or midday. They gorged and fasted at fantastically irregular intervals. One of the sights for tourists to see who were important enough to gain admittance was the king gorging himself on food and drink.

In the fifteenth century a proper feast would consist of brawn (the potted flesh of a boar), bacon and pease, beef, boiled chicken, roast goose, roast pig, veal, lamb, fritters, spiced apples and pears bread and cheese, spiced cakes and wafers, washed down with bragot (made from ale, honey, and spices), and mead (fermented honey water). Feasts were frequent and invariably enormous. But it was considered ill-mannered to cram the face like an ape or to wipe the teeth on the tablecloth!

However, we need not go that far back to find eating that was eating. Americans were quite accomplished in the gentle art of making food vanish, even a couple of generations ago. Nor was this, as some carping critics have declared, merely an attack upon a monotonous round of badly cooked victuals. Even in Colonial days there were berries and fresh fruits in plenty, turnips, parsnips, carrots, fat hogs, kids, venison, poultry, and partridges—at least for the wealthier classes.

But, in Maryland, Delaware, and Virginia, the poor tended to subsist too largely on corn, beef or salted pork, kidney beans, and a few coarse vegetables. Yet between 1800 and 1860 meals at inns varied from a profusion of ham, eggs, fritters, butter, and tea to mere bacon, eggs, hominy, coarse bread, and rum. But even the caustic Frances Trollope and the not wholly unastringent Charles Dickens declared that they got a great deal of good food in these United States.

Around 1860 all the present kinds of meat and fowl abounded and Americans ate more meat per capita than ever after. The 1830-39 rate was 178.7 pounds annually per capita; it rose to 183.9 pounds in the 1850-59 period, but fell to 128.6 in 1930-39. During these same periods wheat flour consumption ran 170, 205, and 158 pounds, respectively, and that of sugar started at 13.1, rose to 29.7 in 1850-59, and was 95.5 pounds per capita per year in 1930-39.

Before and up to the Civil War there was much unoccupied land that could be used for grazing, so livestock abounded. Mrs. Trollope mentions seeing excellent beef, mutton, and veal available in the markets of Cincinnati at 4 cents a pound—in 1828-30. Chickens ready for the table were 12 cents each, regardless of size, but cost less if purchased alive. Turkeys and geese were 50 cents apiece. But fruits and vegetables tended to remain high in price and to be infrequently used between 1800 and 1860.

In those days, to tell the truth, cooking was rather unscientific and dyspepsia abounded. Department of Agriculture reports mention this during the 1860's. Foreign visitors often commented on the carniverous Americans, who wolfed their food. But a hotel room with four or five big meals cost only \$2.50 daily, while boarding houses provided rooms and enormous meals at \$5 a week. Of what did such meals consist?

Breakfasts usually consisted of several kinds of bread, pancakes, fritters, butter, molasses, preserves, hot beefsteaks, roast and boiled chickens, various cold meats, coffee, milk, or chocolate. For dinner the starved guest met up with chicken pie, veal pie, beefsteaks, roast lamb, roast mutton, roast veal, mutton cutlet, boiled ham, pigeons, roast pork, peas, beans, hominy, potatoes, sweetpotatoes, corn on the cob, turtle soup, pie, stewed fruits, beverages, and nuts—all on the same menu and served at the same meal in modest inns.

However, by 1900 our diet revolved around large quantities of meat also—beef stood first with pork second—sweets, white flour products, potatoes, cabbage, and onions. Fresh fruits and vegetables were served in summer but seldom, except apples, in winter. W. O. Atwater, founder of American nutrition science, thought the

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American diet too one-sided and said we were a race of fat, starch, and sugar eaters. Yet he extolled the codfish, potato, pork, and bean diet of New England.

But where are the big meals of yesterday now? You sometimes come upon them as the writer did in Northern Georgia in 1946 where he ate a breakfast consisting of cereal, eggs, bacon and sausage in unlimited quantities, all the hot rolls and coffee he could consume, and a dinner at which two salads, six vegetables, and two meats were served, boarding-house style, with rolls and coffee ad lib. and generous dessert. The breakfast cost 50 cents, the dinner 75, but don't start down there. It's a very small village.

It was even a very small inn. It is not customary for restaurants, boarding houses, or hotels to serve such meals these days. Moreover you probably do not eat that way even in your own home. What has come over the American diet? What changes have occur-

red since the turn of the century?

Broadly speaking the newer knowledge of nutrition has been adopted in practice. Meals that include just a few appetizing and well-cooked dishes, carefully planned to provide all the nutritive essentials, are more common now than groaning tables which may later pass the groans along to those who eat thereat, in the form of upset stomach. Surveys have shown that such meals are common. They are also economical, easier to prepare and clean up after, and scientifically sound.

For instance a recent study made in Mississippi shows that homemakers spent only 3 hours and 18 minutes a week, or about 28 minutes daily, preparing breakfasts at which fewer than five dishes were served, but it required an average of 3 hours and 48 minutes weekly—an additional 28 hours a year—if the breakfasts consisted of more than five dishes. Moreover, cleaning up on the five-dish breakfasts took only 3 hours and 18 minutes a week, while the job lasted 3 hours and 24 minutes weekly for meals of more than five dishes.

It was the same with dinner. If fewer than five dishes were served—and a well-balanced, appetizing, nourishing meal can be so prepared—preparation averaged 9 hours weekly; with more than five dishes, 12 hours weekly. Clearing away and cleaning up took 3 hours and 54 minutes weekly for dinners of fewer than five dishes and 4 hours and 24 minutes for those of more than five.

This marks a broad trend. Here are some detailed facts to back it up, discovered when the Bureau of Human Nutrition and Home Economics studied the American diet from 1909 until 1945, results just published. Throughout this 37-year period the calcium, riboflavin, and vitamins A and C steadily increased. Protein, iron, niacin, and thiamine declined from 1909 until the midthirties, then took an upward swing with increasing meat consumption and enriched grain products.

Due solely to enrichment, the 1945 food supply offered 17 per cent more iron, 27 more thiamine, 12 more riboflavin, and 19 more niacin than before the war. In 1945, Americans had more eggs, dairy products, citrus fruits, and vegetables per person than ever before. In addition the per capita meat supply was the greatest since 1909, except for the peak year, 1911.

The most notable changes in food consumption during the 1909-45 period were steady increases in the use of dairy products, butter excluded, of citrus fruit, and of leafy green and yellow vegetables. There were accompanying downward trends in per capita consump-

tion of potatoes and of grain products.

Egg consumption rose steadily during the 1920's, then declined until 1930, then began to rise again. Consumption of fats and oils, bacon and salt pork included, leveled off about 1923, when it had attained a somewhat higher point than in 1909. Except as influenced by war, butter consumption fluctuated little. New records were set in both war periods for consumption of dry beans, peas, and nuts. No definite trend is apparent in the consumption of fruits and vegetables other than those already mentioned above.

But there was a decline of one-third in per capita consumption of grain products, 1909 to 1945. Much of this was attributable to decreased use of wheat flour, though consumption of both corn and rye declined. However, consumption of breakfast foods increased materially. There was also an upward trend in sugar consumption from 1909 until 1930, then a decline, followed by a sharp rise in 1941, with a subsequent decline due to short supplies and rationing.

Between 1909 and 1945 the potential calories supplied by our per capita food supply ranged from 3,170 to 3,560 apiece daily. Until 1931 the daily average was usually above 3,400; it fell to 3,170 in 1935, but rose to 3,300 during World War II. While the amount of carbohydrate in our diet has rather steadily declined, largely

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because of the decline in potato consumption and in the use of grain products, the calories have risen because of increases in fat available in visible and in invisible—say in milk—form.

Per capita protein supplies in our food supply decreased rather steadily between 1909 and 1933, took an upward turn in 1934 because droughts made it necessary to kill off so much livestock, then, in 1935, dropped to the low for the 35 years, 85 grams per capita per day. Since 1935 protein has rather steadily increased to 101 grams per capita in 1945, which is just where we started in 1909. Protein increases have come in large part from increased use of milk, eggs, poultry, and fish.

The calcium in our diet has risen steadily. Iron, thiamine, and niacin tended to follow the protein curve, declining from 1909 until the midthirties, then rising, but the general trend of riboflavin was upward all along. The food-enrichment program served to improve our iron intake, but even without it, dietary changes alone would have given us 15 per cent more in 1945 than in the 1935-39 period.

The vitamin A content of the American diet has risen quite steadily since 1925, the highest value yet recorded, 9,900 International Units per capita per day, being for 1945. Victory Gardens and the increased use of leafy green and yellow vegetables helped boost this figure from a mere 7,100 I. U. in 1925.

The amount of vitamin C or ascorbic acid in our diet fluctuated, but showed a slight upward trend from 1909 until the early 1930's. Then it underwent a period of accelerated increase until the 1940 level was 40 per cent above that of 1930. Again some of this increase may be attributed to the popularity of Victory Gardens.

Speaking more broadly, and turning now to an article by Dr. F. A. Harper of Cornell, published in *Farm Economics* during 1942, we averaged 1,877 pounds of food each in the 1909-13 period and 1,839 in 1935-39. But the nutrients in this food averaged only 787 and 679 pounds, respectively. So we used 14 per cent less food by weight, per capita, in the later than in the earlier period.

During this interval our consumption of cereals slumped 32, of potatoes 23, and of meat 13 per cent. But we consumed 12 per cent more fruits, 11 more vegetables other than potatoes, 35 more dry beans, 19 more dairy products, 9 more eggs, 21 more sugar, 16 more fats and oils, and 214 per cent more nutriment in the form of beverages—probably indicating the carbohydrates in soda pop.

In general we got 5 per cent fewer calories. We ate 17 per cent less carbohydrates, 2 more fats, 16 less protein, 11 less ash or minerals, and 2 per cent more refuse and fiber—still comparing the

periods 1909-13 and 1935-39.

Then, right during the war, the executive director of the National Grocer's Institute told a session of the National Delicatessen Show in New York City that we wasted from 25 to 50 per cent of our food. He estimated that 50 per cent of the nutritive value of canned goods was poured down kitchen sinks in ignorance of proper culinary processes. Then he attributed the 24 million work days lost through illness in one month very largely to poor diet. We might well chew mentally on these facts as we reline our stomachs three times daily.

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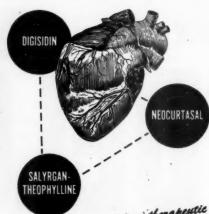
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